

# Reactions with Coumarinohydrazidoyl Halides: Synthesis of Some New Coumarinoyl Pyrazole and 1,2,4-Triazole Derivatives via Dipolar Cycloaddition Reactions

Nabila A. Ismail<sup>1</sup>, Sanaa M. Eldin<sup>2</sup> and Rida M. Fikry<sup>1</sup>

<sup>1</sup>Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Egypt, <sup>2</sup>National Research Center, Dokki, Giza, Egypt

(Received March 4, 1993)

Several new coumarinoyl pyrazole and coumarinoyl-1,2,4-triazole derivatives were synthesised via dipolar cycloaddition reactions with 3-coumarinohydrazidoyl halide. Structure were based on elemental analysis and spectral data.

**Key words:** Coumarin, Hydrazidoyl halides, Pyrazoles, 1,2,4-triazoles, Cycloaddition reactions

## INTRODUCTION

Interest in the synthesis and chemistry of hydrazidoyl halides has revived during the last few years. In this respect, we have recently published a series of publications (Ismail, 1991a,b; Ismail *et al.*, 1991) dealing with the subject. As a continuation to the effort done in this field it was thus decided to extend our investigations to cover the area of cycloaddition reaction with nitrilimines derived from coumarinoyl hydrazidoyl halides. The newly synthesised heterocyclic derivatives contain both the coumarin ring and the pyrazole or 1,2,4-triazole ring which make them highly promising for both biological activity studies (Mathur *et al.*, 1965; Cingolani *et al.*, 1969; Essawy *et al.*, 1980; Fliege *et al.*, 1984) as well as for further chemical transformations leading to other heterocycles.

## MATERIALS AND METHODS

All melting points are uncorrected. IR (KBr) were recorded on a pye Unicome Sp. 1100 spectrometer. <sup>1</sup>H-NMR spectra were recorded in DMSO-d<sub>6</sub> on a Varian EM 390 90 MHz spectrometer using TMS as an internal standard and chemical shifts are expressed as  $\delta$  ppm units. The microanalyses were performed at the Microanalytical Center of Cairo University using Perkin-Elmer 2400 CHN Analyzer.

Compound **1** was prepared according to literature procedure (Ismail *et al.*, 1991), which equivalent

amount of triethylamine to give the corresponding nitrilimine **2**, which was taken as the starting material. Compound **2** reacted with Schiff base, ethyl acrylate, acrylonitrile, N-phenyl maleimide and some  $\alpha,\beta$  unsaturated nitriles, according to the following procedure.

## General Procedure

A solution of **1** (0.01 mole) in dry benzene was treated with (0.01 mole) of triethylamine dropwise with stirring. After complete addition (30 min.) each reagent (0.01 mole) was added and the reaction mixture was when refluxed for 3 h. The solid products which separated after cooling were filtered off and washed with petroleum ether, then crystallized from the proper solvents to give the new compounds listed in (Table I).

## RESULTS AND DISCUSSION

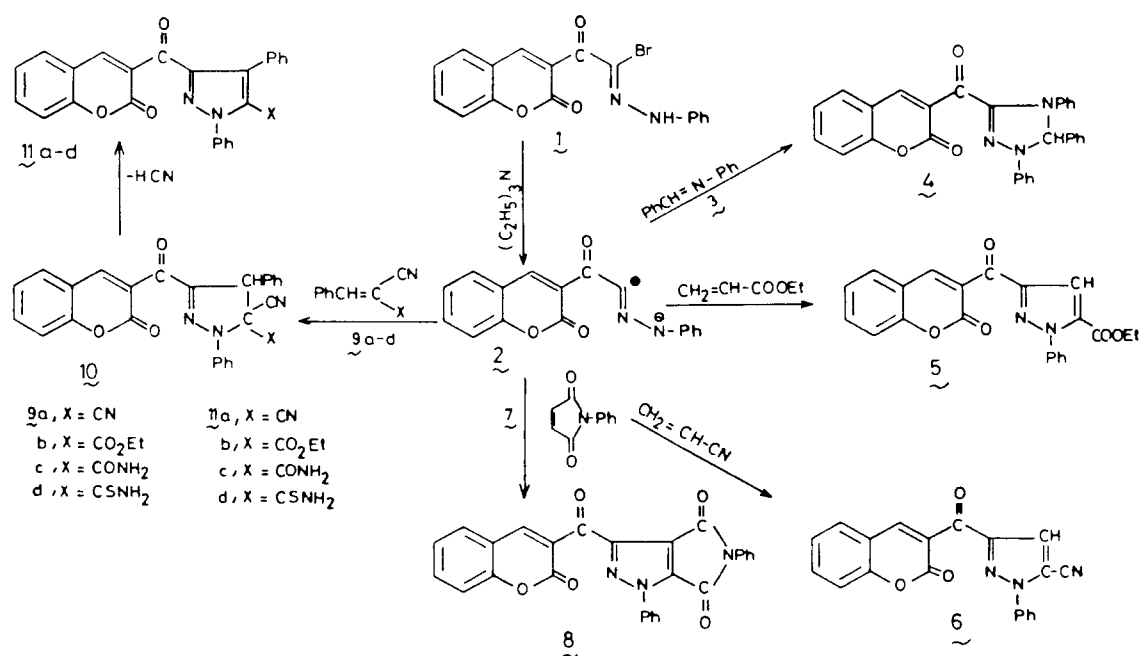
Thus it has been found that  $\alpha$ -(3-coumarinyl)- $\beta$ -bromoglyoxal- $\beta$ -phenyl hydrazone (**1**) (Ismail *et al.*, 1991) reacted with the equivalent amount of triethylamine to generate the corresponding nitrilimine **2** which was taken as the starting material for the present study.

Compound **2** reacted also with ethyl acrylate to afford a reaction product which was formulated as 3-(3'-coumarinoyl)-5-ethoxy carbonyl-pyrazole **5**. Structure of **5** was established on the basis of correct elemental analysis and spectral data. IR spectrum of **5** showed bands at 1690, 1670, 1650 of (three CO) groups in addition to a band at 1620 of (C=N) group. The <sup>1</sup>H-NMR spectrum revealed the presence of the CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub> group (t, 3H, 1.3 and q, 2H, 4.3) in addition to a multiplet at 6.8-7.4 corresponding to pyrazole H-

Correspondence to: Nabila A. Ismail, Department of Chemistry, Faculty of Science Zagazig University, Zagazig, Egypt.

**Table I.** Characterization data of the newly synthesized derivatives

Comp.	Colour (solvent)	M.P. (°C)	Yield (%)	Mol. Formula	% Analysis		Calcd./Found	
					C	H	N	S
<b>4</b>	Brown (benzene)	260	60	C <sub>30</sub> H <sub>21</sub> N <sub>3</sub> O <sub>3</sub>	76.4	4.6	8.9	
					76.2	4.4	8.7	
<b>5</b>	Orange (CCl <sub>4</sub> )	145	60	C <sub>22</sub> H <sub>17</sub> N <sub>2</sub> O <sub>5</sub>	67.8	4.4	7.2	
					67.6	4.2	7.0	
<b>6</b>	Brown (ethanol)	220	60	C <sub>20</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub>	70.4	3.2	12.3	
					70.2	3.2	12.1	
<b>8</b>	Brown (ethanol)	185	60	C <sub>27</sub> H <sub>15</sub> N <sub>3</sub> O <sub>5</sub>	70.3	3.3	9.1	
					70.1	3.1	9.0	
<b>11a</b>	Orange (tolouene)	210	50	C <sub>26</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub>	74.8	3.6	10.1	
					74.6	3.5	10.0	
<b>11b</b>	Orange (tolouene)	150	50	C <sub>28</sub> H <sub>20</sub> N <sub>2</sub> O <sub>5</sub>	72.4	4.3	6.0	
					72.2	4.1	6.0	
<b>11c</b>	Orange (tolouene)	180	50	C <sub>26</sub> H <sub>17</sub> N <sub>3</sub> O <sub>4</sub>	71.7	3.9	9.7	
					71.5	3.7	9.5	
<b>11d</b>	Orange (tolouene)	160	50	C <sub>26</sub> H <sub>17</sub> N <sub>3</sub> O <sub>3</sub> S	69.2	3.8	9.3	7.1
					69.0	3.7	9.1	6.9

**Scheme 1**

4, coumarinoyl and aromatic protons (11H). The disappearance of any signal in the region of  $\delta$  4.5-6.5 ppm proves that the compound suffered dehydrogenation under the applied reaction conditions.

Similar to its behaviour towards ethyl acrylate, compound **2** reacted with acrylonitrile to yield the dipolar cycloaddition reaction **6**. IR of **6** showed the presence of bands at 1680, 1660 of (two CO) and a band at 2220 of (CN). <sup>1</sup>H-NMR spectrum revealed the presence of signals of pyrazole H-4 (s, 6.6) in addition to

the multiplet ( $\delta$  6.8-7.5 ppm) corresponding to coumarinoyl and aromatic protons (10H). These results proved that the reaction product suffered also dehydrogenation under the applied reaction conditions. The possibility that both **5**, **6** could be the corresponding 4-substituted derivatives was readily ruled out based on the data previously reported by several investigators (Tewari *et al.*, 1983a,b; Ezmirly *et al.*, 1988; Shawali *et al.*, 1990).

Furthermore, **2** cycloadded to N-phenyl-maleimide

7 in dry benzene and the reaction product was formulated as 1,5-diphenyl-1-3-coumarinoyl pyrrolino(3,4-c) pyrazole-2,6-dione **8**. Compound **8** gave the absorption bands of two CO groups in its IR spectrum in addition to the two widely separated bands at 1780 and 1710  $\text{cm}^{-1}$  characteristic for the (-CO-NR-CO) grouping. Its  $^1\text{H-NMR}$  did not reveal except the multiplet at 6.8-7.6  $\delta$  ppm corresponding to coumarinoyl and aromatic protons. This result proved the dehydrogenation of the reaction product under the applied reaction conditions.

The course of cycloaddition of some  $\alpha,\beta$ -unsaturated nitriles **9** was also investigated. Thus, it has been found that **9a-d** reacted with **2** to yield cycloaddition reaction products with a molar ratio of 1:1. These reaction products could then be formulated as the 4-phenyl-5-substituted pyrazole derivatives **11a-d** respectively. The IR spectrum of each **11a-d** did not show any nitrile absorption. The disappearance of any signals for pyrazols protons in the  $^1\text{H-NMR}$  spectra of these products indicated that these products were dehydrocyanated under the applied reaction conditions as compounds **11a-d** were assumed to be formed via initial formation of the addition products **10a-d** respectively which lost HCN to yield the final isolable **11a-d** respectively. Again the regioselectivity problem was solved and structures were established to be the 1,4-diphenyl pyrazole derivatives rather than the isomeric 1,5-diphenyl pyrazole based on previous reports in this respect (Tewari *et al.*, 1983a,b; Ezmirly *et al.*, 1988; Shawali *et al.*, 1990).

## REFERENCES CITED

- Cingolani, G. M., Gualtieri, F., and Pignini, M., Research in the field antiviral compounds Mannich bases of 3-hydroxy coumarin. *J. Med. Chem.*, 12, 531-532 (1969).
- Essawy, A. I., Elkady, M. and Mohamed, A. Y., Some reactions of 3-cinnamoylcoumarins. *Indian J. Chem.*, 19B, 567-570 (1980).
- Ezmirly, S. T. and Shawali, A. S., The regioselectivity in the reactions of N-aryl-C-ethoxy carbonyl nitrilimines with acrylic acid derivatives. *J. Heterocyclic Chem.*, 25, 257-263 (1988).
- Fliege, W., Grashy, R. and Huisgen, R., 1,3-Dipolare cycloaddition. Die Chemie des N-Methyl-C-Phenyl nitrilimines. *Chem. Ber.*, 117, 1194-1214 (1984).
- Ismail, N. A., Reactions with coumarinohydrazidoyl halides: Synthesis of several new coumarin, 1,3,4-thiazole, Benzo-1,4-oxazine and benzo-1,4-thiazine derivatives. *Egypt J. Pharm. Sci.*, 32, 961-970 (1991).
- Ismail, N. A., Reactions with coumarin derivatives: Synthesis of several new coumarinopyrazoles, coumarinopyridines and coumarinyl azoles. *Egypt J. Pharm. Sci.*, 32, 685-693 (1991).
- Ismail, N. A., Khalifa, F. A. and Magd El-Din, A. A., Reactions with coumarins: Synthesis of several new annelated pyridine and pyrrolylocoumarin derivatives. *Heterocycles*, 32(6), 1101-1107 (1991).
- Koelsch, C. F., Bromination of 3-acetocoumarine. *J. Am. Chem. Soc.*, 72, 2993-2995 (1950).
- Mathur, C. N., Mitra, C. R., Krishnaswamy, N. R., Kulshreshtha, R. K. and arora, R. B., Effect of some coumarin derivatives on the coronary flow and their structure-activity relation. *Arch. Intern. Pharm.*, 153(1), 218-225 (1965).
- Shawali, A. S., Hassaneen, H. M., Ibrahim, H. A., Mekki, S. T. and Fahmi, A. A., Synthesis and cycloaddition reactions of N-aryl-2-furohydrazonyl chlorides. *Arch. Pharm. Res.*, 13(2), 126-131 (1990).
- Tewari, R. S. and Parihar, P., 1,3-Dipolar cycloaddition and nucleophilic substitution reaction of C-acetyl and C-ethoxy. Caronyl derivative of hydrazidoyl bromides. *Tetrahedron*, 39(1), 129-136 (1983).
- Tewari, R. S., Dixit, P., Dubey, D. and Ajoy, K., Studies on 1,3-dipolar cycloaddition reactions of some cycloimmonium ylides. *J. Chem. Eng., Data*, 28, 283-285 (1983).